

REMARKS

**35 U.S.C. § 112: Claim 1**

The Examiner has raised the objection that claim 1 is indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In response to this objection, claim 1 has been amended to indicate that the device should be sized and shaped to be removably inserted into an individual well of a standard size well plate. Support for these amendments is found on page 5, lines 8-11 and original claims claim 8 and 10.

It is submitted that the size and shape necessary for insertion into a well of a standard size well plate are well known to the person skilled in the art; standard size well plates are very commonly used. The device of claim 1 is therefore clearly defined and Applicant submits that the Examiner's objection has been overcome.

**Formality Objections**

Claims 8, 15, 18 and 20 are objected to on formal grounds. Claims 8 and 20 have been canceled and claims 15 and 18 have been amended. Applicant submits that these amendments overcome the Examiner's objections.

**Prior Art Rejections**

**Claims 1, 3, 8 and 10 are rejected under 35 U.S.C. § 102(b) as anticipated by or in the alternative, under 35 U.S.C. § 103(a) as obvious over Kessler et al. (DE 38 16 489 A1).** Applicant respectfully requests reconsideration of this rejection.

Claim 1 has been amended as discussed in the paragraph above on 35 USC 112. Kessler does not disclose a device that is sized and shaped to be removably inserted within an individual well of a standard size well plate and therefore it is submitted that the device of amended claim 1 is novel over the disclosure of Kessler and that the Examiner's objection has thereby been overcome.

The Examiner has also expressed the opinion that claim 1 of the present application lacks inventive step because it would be obvious to the person skilled in the art that the luminescent device of Kessler is of a size and shape that allows the luminescent device to be housed in a sample holder of a light measuring apparatus. In the light of the amendments filed, this objection is now moot. For the sake of explanation, however, the Applicant submits that amended claim 1 is both novel and inventive over the disclosure of Kessler for the following reasons.

Kessler teaches a luminescent device that is to be positioned in place of a light guide that would normally transmit light from an analyte sample to a photodetector. It does not disclose or suggest that the luminescent device should be placed in a sample holder. In other words, the connection between the analyte sample and the photodetector, that allows measurements to be made, is severed by the removal of the light guide in order to position the luminescent device in the apparatus for calibration. Light emitted by the luminescent device is then detected by the photodetector and used to calibrate the optical instrument. The connection between the sample and the photodetector must be re-established by removing the luminescent device and reconnecting the light guide (pages 6-7 of the translation into English) before measurements can be taken from the analyte sample. Thus, during calibration of the apparatus, testing must be stopped to insert the calibration device into the apparatus. As such, it is not possible to check the

calibration of the machine whilst measuring light output from test samples. There is thus a risk that the accuracy of the apparatus may decrease between calibrations i.e. during testing, so that test results may become less accurate than is desirable. This problem is identified and discussed on page 2, line 24 of the present application.

In contrast to this, the feature of the size and shape of the luminescent device of amended claim 1 provides the advantage that it is small enough to be housed in a single well of a standard size well plate in a luminometer or other scientific apparatus measuring optical output, so that it is possible for the luminescent device to be left in the apparatus during use, even when other wells contain test materials. The accuracy of the scientific apparatus can therefore be checked at each instance of use of the apparatus, with the luminescent device (page 20-23). This has the advantage that it is possible to check the calibration of the machine whilst measuring test samples, so that the accuracy of the apparatus is known at the time of testing and test results remain accurate.

Indeed, it is submitted that the disclosure of Kessler teaches away from the device of the present application, because it teaches that the device should be placed not in a well of a well plate, but should be positioned far from the samples, replacing a light guide prior to a test run (Figure 1 of Kessler). The problems to be addressed by Kessler and the present application are therefore different; the problem to be solved by Kessler is the need for calibration of a photodetector device prior to running a test series, while the problem to be solved by the present invention is how to calibrate a photodetector at the same time as measuring test samples (page 2, lines 27-29).

Furthermore, Kessler does not disclose or suggest a device that can be inserted into a single well of a standard size well plate, nor does it disclose or suggest the advantages obtained from this feature that are discussed above. Indeed, the disclosure of Kessler teaches away from the development of such a device, because it specifies a size of 3mm by 15mm (page 4 of the translated specification), which would be too large to fit inside a well of most standard size well plates. The person skilled in the art would not be led to design a device that is suitable for removable insertion into the well of a standard size well plate after reading this disclosure.

It is therefore submitted that the device of amended claim 1, and all claims depending therefrom, is both novel and inventive over the disclosure of Kessler.

**Claim 2 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of MacHutchin (US 2,953,684).** Applicant respectfully requests reconsideration of this rejection. Claim 2 depends from Claim 1 and is patentable over Kessler for the reasons set forth above. MacHutchin does not cure the deficiencies of Kessler.

**Claim 4 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Linhart (US 3,566,125) and Phillips (US 2,745,738).** Claim 4 has been canceled. Thus, this rejection is moot.

**Claims 5, 7 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Adams (US 6,549,279).** Applicant respectfully requests reconsideration of this rejection. Claims 5, 7 and 12 depend from Claim 1 and are patentable over Kessler for the

reasons set forth above regarding the patentability of claim 1. Adams does not cure the deficiencies of Kessler.

**Claim 6 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Adams and Terashita (US 5,073,008).** Applicant respectfully requests reconsideration of this rejection. Claim 6 depends from Claim 1 and is patentable over Kessler for the reasons set forth above regarding the patentability of claim 1. Neither Adams nor Terashita, when taken alone or in combination, cure the deficiencies of Kessler.

**Claim 11 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Gelman (US 5,389,774).** Applicant respectfully requests reconsideration of this rejection. Claim 11 depends from Claim 1 and is patentable over Kessler for the reasons set forth above regarding the patentability of claim 1. Gelman does not cure the deficiencies of Kessler.

**Claims 13 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Leveille (US 2002/0096667).** Applicant respectfully requests reconsideration of this rejection. Claims 13 and 15 depend from Claim 1 and are patentable over Kessler for the reasons set forth above regarding the patentability of claim 1. Leveille does not cure the deficiencies of Kessler.

**Claim 14 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Leveille, and further in view of Nast (US 4,575,143).** Applicant respectfully requests

reconsideration of this rejection. Claim 14 depends from Claim 1 and is patentable over Kessler for the reasons set forth above regarding the patentability of claim 1. Neither Leveille nor Nast cure the deficiencies of Kessler.

**Claims 16-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kessler in view of Valenta (US 5,321,261).** Applicant respectfully requests reconsideration of this rejection. First, claims 16-19 (claim 20 was canceled) are directed to an apparatus and method comprising the luminescent device of claim 1. These claims therefore depend from claim 1 and are patentable over Kessler for the reasons set forth above regarding claim 1.

Claim 16 – light measuring apparatus

The Examiner has expressed the opinion that, after reading Valenta, it would be obvious to place the device of Kessler in a sample holder in order to calibrate one or more photomultipliers in a luminometer. Applicant respectfully disagrees.

Applicant has amended claim 16 to recite that the luminescent device is removably inserted into an individual well of a standard size well plate housed in a sample holder, and that the apparatus comprises means for obtaining a reading of light output from the luminescent device and means for adjusting the reading of light output to the pre-determined intensity of the light output of the luminescent device. Support for these amendments is found in original claim 15 and page 5, lines 11-23 of the specification.

Applicant submits that the apparatus of amended claim 16 is both novel and inventive over the disclosure of Valenta and Kessler, either separately or in combination. A device with the

combination of features of amended claim 1 is not, as discussed above, disclosed or suggested by Kessler and is therefore novel and inventive. Claim 16 is dependent on amended claim 1 and therefore, although Valenta may disclose the use of a light standard fixed within a well, this reference cannot overcome the deficiencies of the disclosure of Kessler in order to anticipate or render obvious the present apparatus claim 16.

The light standard of Valenta is comprised of a mixture of a scintillator, a binding material and a radioactive material permanently fixed at the bottom of a well of a standard well plate, being sealed in the well by the use of a binder and a potting material (column 5, lines 14-17). Such a standard is therefore permanently attached within the well, and is disposable because it is discarded along with the standard size well plate. In contrast to this, the apparatus of claim 15 includes a light emitting substance that is sealed within a housing and a magnetic outer casing and which may be removably inserted into the well of a standard size well plate. This feature has numerous advantages for the user. For example cost-effectiveness may be improved, because it is not necessary to continuously use reagents to make disposable standard size well plates including new standards. The light source will not be at any risk of contamination, because it is sealed within a housing. In addition, because the housing is transparent, the light source will not be obscured, for example by the presence of a potting material etc. Furthermore, it is very convenient to have a single light source according to the invention that may be removed and subsequently used in multiple experiments, in different standard sized well plates.

The disclosure of Valenta also teaches that an apparatus for calibrating an instrument requires “means for successively counting photon emissions of a standard by two or more photodetectors, at least one of the photodetectors being the reference detector...means for

calculating a counting ratio...means for multiplying the counts of a luminescent sample subsequently measured by a particular photometer by the inverse of said counting ratio computed for that particular photometer” (claim 20 of Valenta). Amended claim 16, in contrast to this, claims an apparatus including means for obtaining a reading of light output from the luminescent device; and means for adjusting the reading of light output of the apparatus to the pre-determined intensity of the light output of the luminescent device. The apparatus of Valenta teaches away from the present invention, because the person skilled in the art would be led to develop an improved method of comparing the accuracy of one photomultiplier with another, rather than to develop an apparatus of the present invention, in which the reading of the light output is adjusted to the intensity of a predetermined light source.

The combination of features of amended claim 16, or the advantages resulting therefrom, is not disclosed or suggested by Kessler or Valenta, either alone or in combination. Therefore, it is submitted that amended claim 16 is both novel and inventive over these two cited prior art documents.

Claim 18 – method of analyzing a sample

The Examiner has expressed the opinion that, after reading Valenta in the light of Kessler, method claim 18 is rendered obvious. Applicant has amended claim 18 to recite steps (a) through (f). Support for these amendments is found in original claims 18 and 20, and on page 5, lines 11-23.

The method of Kessler does not disclose or suggest the analysis of a sample using a device as claimed in amended claim 1. The arguments for novelty and inventive step for the

device of claim 1 apply equally to the novelty and inventive step of the present method of analysis of a sample. Briefly, the method of the present invention allows for the apparatus to be checked for accuracy of light detection at the same time as the test samples are being measured.

Valenta is known to the applicant and it discloses a method for normalising photodetectors, by counting efficiencies between two or more photodetectors and adjusting the count of one photodetector to correspond to the count of another photodetector (column 1, lines 34-37) in which each photomultiplier component of the multi-photomultiplier is calibrated against another photomultiplier in the same photomultiplier (page 3, lines 3-6). For this method, therefore, one photodetector is required for use as a reference. No absolute measurement is taken; the object of this prior art apparatus is to ensure that each photodetector is calibrated relative to each other, so that no matter which photodetector is used to make a measurement, the reading will be the same.

The method of analysing a sample of the present invention has the advantage over the prior art that the equipment to be tested is compared to a light source of pre-determined intensity rather than being tested relative to another photomultiplier. The method of analysis of the present invention, therefore, provides for simultaneous calibration of the machine and testing of samples, for maximal apparatus measuring accuracy. Neither document discloses or suggests, alone or in combination, a method of analysing a sample with the combination of features of amended claim 16, wherein the luminescent device is left in the apparatus during use so that the calibration of the machine may be tested whilst measuring the analyte sample. Applicant respectfully submits, therefore, that amended claim 16 is both novel and inventive.

Claim 20 – method for calibrating an apparatus

Original claim 20 has been canceled. New claim 22 is directed to a method for calibrating an apparatus. The Examiner has expressed the opinion that the method of calibrating an apparatus as described in original claim 20 is obvious over Kessler in view of Valenta. The Examiner has also stated that Kessler discloses a method comprising adjusting the reading of light output of the apparatus to the measured pre-determined intensity of the light output of the luminescent device placed in the apparatus.

New claim 22 is dependent on amended claim 16, which includes the features that the luminescent device of claim 1 is positioned in a well of a standard size well plate, the standard size well plate being housed in a sample holder of the apparatus. Support for this claim may be found in the description at page 5, lines 11-23. The advantage of this feature is that the calibration of the machine may be tested whilst measuring the analyte sample. This avoids the risk that accuracy of the apparatus may decrease between calibrations i.e. during testing.

Kessler discloses a method of calibration of a light measurement device in which the calibration takes place prior to the start of a test series. Valenta does not disclose or suggest a method in which the luminescent device is left in the apparatus during use so that the calibration of the machine may be tested whilst measuring the analyte sample. The risk of decreased accuracy in between calibrations is, therefore, not avoided in the methods disclosed by either Kessler or Valenta, either alone or in combination.

In addition, Valenta, as discussed above, discloses a method in which each photomultiplier component of the multi-photomultiplier is calibrated against another photomultiplier in the same photomultiplier (page 3, lines 3-6). The method of the present

invention has the advantage that the equipment is calibrated by adjusting the reading of light output of the apparatus to the pre-determined intensity of the light output of the luminescent device. This is in contrast to the disclosure of Valenta, in which each photomultiplier is tested relative to another photomultiplier (Abstract). In other words, the calibration of the machine according to the present invention is absolute, because it is compared to a light standard of known light intensity. This helps to avoid any inaccuracies that may occur as a result of testing photomultipliers relative to each other.

Kessler does not disclose or suggest the advantageous combination of features of new claim 22, and therefore it is respectfully submitted that the subject matter of this claim is novel and inventive over the cited document.

In view of the foregoing, Applicant submits that the Examiner's objections have been overcome and that this application is in condition for allowance. Should any issue remain to be resolved, Applicant requests that the Examiner telephone the undersigned.

Dated: July 2, 2008

Respectfully submitted,

**Customer No. 44702**  
**OSTRAGER CHONG FLAHERTY**  
**& BROITMAN P.C.**

By: /joshua s. broitman/  
Joshua S. Broitman  
Reg. No. 38,006

570 Lexington Avenue, 17<sup>th</sup> Floor  
New York, New York 10022-6894  
(212) 681-0600  
Attorneys for Applicant